

WHAT IS CLAIMED IS:

1. A method for detecting a hepatic cell proliferative disorder, comprising:
detecting a methylated CpG-containing glutathione-S-transferase (GST) nucleic acid in a hepatic specimen or biological fluid wherein a methylated GST nucleic acid is indicative a hepatic cell proliferative disorder.
2. The method of claim 1, wherein the GST nucleic acid is detected by contacting the nucleic acid with nucleic acid primers.
3. The method of claim 2, wherein the primers flank a region in the promoter of GST.
4. The method of claim 3, wherein the promoter region is approximately -539 to --239 upstream from the start site.
5. The method of claim 2, wherein the nucleic acid primers are selected from the group consisting of SEQ ID NO:1, 2, 7, 8, 9, 10, 11, 12, 13, and combinations thereof.
6. The method of claim 1, wherein the detecting comprises contacting a nucleic acid-containing hepatic specimen or biological fluid with an agent that modifies unmethylated cytosine,
amplifying the CpG-containing nucleic acid in the specimen by means of CpG-specific oligonucleotide primers, wherein the oligonucleotide primers distinguish between modified methylated and nonmethylated nucleic acid, and
detecting the methylated nucleic acid based on the presence or absence of amplification products produced in said amplifying step.
7. The method of claim 6, wherein the amplifying step is the polymerase chain reaction (PCR).
8. The method of claim 6, wherein the oligonucleotide primers have a sequence as set forth in SEQ ID NO: 7, 8, 9, 10, 11, 12, or 13.

9. The method of claim 6, wherein the modifying agent is bisulfite.
10. The method of claim 6, wherein cytosine is modified to uracil.
- Sub D5 > 11. The method of claim 1, wherein the CpG-containing nucleic acid is a promoter region.
12. The method of claim 1, wherein the specimen is from a hepatic tissue.
13. The method of claim 1, wherein the biological fluid is bile or blood.
14. The method of claim 6, further comprising contacting the nucleic acid with a methylation sensitive restriction endonuclease.
15. The method of claim 14, wherein the restriction endonuclease is selected from the group consisting of *MspI*, *HpaII*, *BssHII*, *BstUI* and *NotI*.
- Sub D6 > 16. The method of claim 1, wherein the detecting is by contacting a target nucleic acid in the hepatic specimen or biological fluid with a reagent which detects methylation of the promoter region of the GST when the target nucleic acid is DNA, or wherein the reagent detects the level of GST RNA when the target nucleic acid is RNA; and detecting the GST target nucleic acid, wherein hypermethylation of the promoter of GST DNA, or decreased levels of GST RNA, as compared with the level of GST RNA in a normal cell, is indicative of a GST-associated cell proliferative disorder in hepatic tissue.
17. The method of claim 16, wherein the reagent is a nucleic acid primer selected from the group consisting of SEQ ID NO:1, 2, 7, 8, 9, 10, 11, 12, 13, and combinations thereof.
- Sub D7 > 18. The method of claim 1, wherein the GST is a π family GST.
19. The method of claim 18, wherein the π family GST is GSTP1.
- Sub D8 > 20. The method of claim 16 wherein the reagent which detects methylation of the promoter region of the GST is a restriction endonuclease.

21. The method of claim 20, wherein the restriction endonuclease is methylation sensitive.
22. The method of claim 21, wherein the restriction endonuclease is selected from the group consisting of *MspI*, *HpaII*, *BssHII*, *BstUI* and *NotI*.
23. The method of claim 16, wherein the reagent is a nucleic acid probe.
24. The method of claim 23, wherein the probe is detectably labeled.
25. The method of claim 24, wherein the label is selected from the group consisting of a radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, and an enzyme.
26. The method of claim 1, further comprising detecting the presence of hepatitis B virus or hepatitis C virus.
- Sub D9 > 27. The method of claim 1, further comprising comparing the methylation status of the GST to adjacent normal hepatic tissue.
28. A method for detecting a hepatic cell proliferative disorder associated with a glutathione-S-transferase (GST) in a subject comprising:

 contacting a target nucleic acid in a sample of hepatic tissue or biological fluid from the subject with a reagent which detects the GST, wherein the reagent detects methylation of the promoter region of the GST when the target nucleic acid is DNA, and wherein the reagent detects the level of GST RNA when the target nucleic acid is RNA; and

 detecting the GST target nucleic acid, wherein hypermethylation of the promoter of GST DNA, or decreased levels of GST RNA, as compared with the level of GST RNA in a normal cell, is indicative of a GST-associated cell proliferative disorder in hepatic tissue.
29. The method of claim 28, wherein the GST is a π family GST.
30. The method of claim 29, wherein the π family GST is GSTP1.

31. The method of claim 28, wherein the biological fluid is bile or blood.
32. The method of claim 28, wherein the reagent which detects methylation of the promoter region of the GST is a restriction endonuclease.
33. The method of claim 32, wherein the restriction endonuclease is methylation sensitive.
34. The method of claim 33, wherein the restriction endonuclease is selected from the group consisting of *MspI*, *HpaII*, *BssHII*, *BstUI* and *NotI*.
35. The method of claim 28, wherein the reagent is a nucleic acid probe.
36. The method of claim 35, wherein the probe is detectably labeled.
37. The method of claim 36, wherein the label is selected from the group consisting of a radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, and an enzyme.
38. The method of claim 28, further comprising detecting the presence of hepatitis B virus or hepatitis C virus.
39. The method of claim 28, further comprising comparing the methylation status of the GST to adjacent normal hepatic tissue.
40. A method for detecting a hepatic cell proliferative disorder associated with a glutathione-S-transferase (GST) nucleic acid in a subject, comprising contacting a target cellular component containing a GST nucleic acid with a reagent which reacts with the GST nucleic acid and detecting hypermethylation of the GST nucleic acid, wherein hypermethylation of the GST nucleic acid is indicative of a hepatic cell proliferative disorder.
41. The method of claim 40, wherein the nucleic acid is DNA.
42. The method of claim 40 wherein the nucleic acid is RNA.
43. The method of claim 40, wherein the reagent is a probe.

44. The method of claim 43, wherein the probe is nucleic acid.
45. The method of claim 43, wherein the probe is detectably labeled.
46. The method of claim 45, wherein the label is selected from the group consisting of a radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, or an enzyme.
47. The method of claim 40, wherein the reagent is a restriction endonuclease.
48. The method of claim 47, wherein the restriction endonuclease is methylation sensitive.
49. The method of claim 48, wherein the restriction endonuclease is selected from the group consisting of *MspI*, *HpaII*, *BssHII*, *BstUI* and *NotI*.
50. The method of claim 40, further comprising detecting the presence hepatitis B virus or hepatitis C virus.
51. The method of claim 40, further comprising comparing the methylation status of the GST to adjacent normal hepatic tissue.
52. A method for detecting a hepatic cell proliferative disorder associated with a glutathione-S-transferase (GST) in a subject, comprising contacting a sample from the subject with a reagent that detects GST polypeptide and comparing the level of GST polypeptide in the sample to a control sample wherein a reduce level in the sample is indicative of a hepatic cell proliferative disorder.
53. The method of claim 52, wherein the subject is a mammal.
54. The method of claim 53, wherein the mammal is a human.
55. The method of claim 52, wherein the GST is a π family GST.
56. The method of claim 55, wherein the π family GST is GSTP1.
57. The method of claim 52, wherein the sample is a hepatic tissue sample.

58. The method of claim 52, wherein the sample is a biological fluid.
59. The method of claim 58, wherein the fluid is bile or blood.
60. The method of claim 52, wherein the reagent is an antibody.
61. The method of claim 52, wherein the reagent is detectably labeled.
62. The method of claim 61, wherein the label is selected from the group consisting of a radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, or an enzyme.
63. The method of claim 52, further comprising detecting the presence hepatitis B virus or hepatitis C virus.
64. The method of claim 52, further comprising comparing the methylation status of a GST polynucleotide in the sample to the status in an adjacent normal hepatic tissue.
65. A method for treating a hepatic cell proliferative disorder, comprising contacting a subject in need of such treatment with an agent which increases the expression of a glutathione-S-transferase (GST), thereby treating the hepatic cell proliferative disorder.
66. The method of claim 65, wherein the GST is GSTP1.
67. The method of claim 65, wherein the agent reduces the methylation of a GST nucleic acid sequence.
68. The method of claim 67, wherein the agent is a DNA methyltransferase inhibitor.
69. The method of claim 68, wherein the DNA methyltransferase inhibitor is 5-azadeoxycytidine.
70. The method of claim 65, wherein the agent is a gene delivery vector containing an unmethylated GST nucleic acid sequence.

71. The method of claim 70, wherein the GST nucleic acid sequence is a GSTP1 sequence.
72. The method of claim 70, wherein the vector contains a nucleic acid sequence encoding a GSTP1 polypeptide operably linked to a promoter sequence.
73. The method of claim 72, wherein the promoter sequence is tissue specific.
74. The method of claim 65 wherein the agent induces expression of a GST.
75. The method of claim 74, wherein the agent is sulfoxurain or oltipraz.
76. A kit useful for the detection of a methylated CpG-containing nucleic acid in a GSTP1 promoter comprising carrier means containing one or more containers comprising a first container containing a reagent which modifies unmethylated cytosine and a second container containing primers for amplification of the CpG-containing nucleic acid, wherein the primers distinguish between modified methylated and nonmethylated nucleic acid.
77. The kit of claim 76, wherein the modifying reagent is bisulfite.
78. The kit of claim 76, wherein said reagent modifies cytosine to uracil.
79. The kit of claim 76, wherein the primer hybridizes with a target polynucleotide sequence having the sequence from about -539 to -239 upstream from GSTP1 transcription start site.
80. The kit of claim 79, wherein the primers are SEQ ID Nos: 1, 2, 7, 8, 9, 10, 11, 12, or 13 or any combination thereof.
81. The kit of claim 76, further comprising nucleic acid amplification buffer.
82. Isolated oligonucleotide primer(s) for detection of a methylated CpG-containing nucleic acid wherein the primer hybridizes with a target polynucleotide sequence having the sequence in the region from about -539 to -239 upstream from GSTP1 transcription start site.

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83. The primers of claim 81, wherein the primers SEQ ID Nos: 1, 2, 7, 8, 9, 10, 11, 12, or 13 or any combination thereof.
84. The method as in any of claims 1, 28, 40 or 52, wherein methylation is in one allele.
85. The method as in any of claims 1, 28, 40 or 52, wherein methylation is in both alleles.